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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
A61K 31/47, 31/445, 31/505

A1

(11) International Publication Number: WO 97/45119

(43) International Publication Date: 4 December 1997 (04.12.97)

(21) International Application Number: PCT/EP97/02481

(22) International Filing Date: 15 May 1997 (15.05.97)

(30) Priority Data:
60/018,336 24 May 1996 (24.05.96) US

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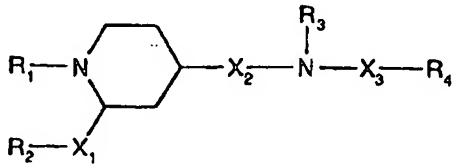
(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

**Published**
*With international search report.*
*Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.*

(54) Title: USE OF SUBSTANCE P ANTAGONISTS FOR TREATING SOCIAL PHOBIA



(I)

(57) Abstract

The invention relates to the use of a compound of formula (I) or of a pharmaceutically utilizable salt thereof, in which $R_1$ is an unsubstituted or substituted aralkyl, aryloxyalkyl, heteroaralkyl, aroyl, heteroaroyl, cycloalkylcarbonyl, aralkanoyl, heteroarylalkanoyl, aralkoxycarbonyl or arylcarbamoyl radical or the acyl radical of an α-amino acid which is unsubstituted or N-substituted by lower alkanoyl or carbamoyl-lower-alkanoyl; $R_2$ is cycloalkyl or an unsubstituted or substituted aryl or heteroaryl radical; $R_3$ is hydrogen, alkyl, carbamoyl or an alkanoyl or alkenoyl radical which is unsubstituted or substituted by carboxyl or esterified or amidated carboxyl; $R_4$ is an unsubstituted or substituted aryl or unhydrogenated or partially hydrogenated heteroaryl radical; $X_1$ is methylene, ethylene, a direct linkage, a carbonyl group which may be ketalized, or an unetherified or etherified hydroxymethylene group; $X_2$ is alkylene, carbonyl or a direct linkage; and $X_3$ is carbonyl, oxo-lower-alkylene, oxo(aza)-lower-alkylene or an alkylene radical which is unsubstituted or substituted by phenyl, hydroxymethyl, carboxyl which may be esterified or amidated, or by hydroxyl in a position higher than α; for producing pharmaceutical products for the treatment of social phobia.

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# USE OF SUBSTANCE P ANTAGONISTS FOR TREATING SOCIAL PHOBIA

## Background of the invention

Tachykinins can be assigned to a family of peptides which have a common Phe-X-Gly-Leu-Meth-$NH_2$ C terminal sequence. One representative of this class of substances is called substance P which, as neurotransmitter or neuromodulator, has a high affinity for the neurokinin-1 ($NK_1$) receptor. Tachykinins are widespread in the central and peripheral nervous systems. Substance P antagonists are attributed with a valuable range of therapeutic properties. For example, it has emerged that substance P antagonists have a pronounced antiasthmatic and anxiolytic effect. The aim of further intensive efforts is to find potential further therapeutic uses of substance P antagonists able to round off the favourable profile of action of such antagonists.

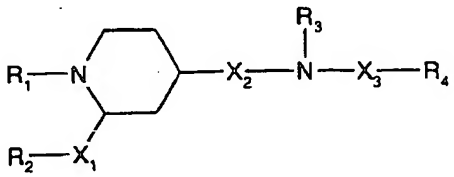
## Description of the invention

There is a pressing need in medicine to find an effective approach to the therapy of the two widespread pathological manifestations of panic disorder and social phobia. According to the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DMS) there is a clear-cut distinction between panic and anxiety disorders. Panic disorder is manifested by discrete unexpected panic attacks, most of which are not caused by external stimuli. Only when such attacks occur with a certain frequency and regularity can they be reliably assigned to the phenomenon of panic disorder. The DSM-III-R criteria, for example, mandate e.g. for the panic disorder condition at least four attacks in 4-week period or one severe attack followed by at least a month of persistent fear of having another attack. Corresponding DSM-III criteria for social phobia include e.g. a persistent, irrational fear of, and compelling desire to avoid, a situation in which the individual is exposed to possible scrutiny by others and fears that the individual may act in way that will be humiliating or embarrassing.Social phobia is diagnosed when an individual has a central anxiety about, for example, appearing ridiculous in public or getting into embarrassing situations, and if the person, through avoiding such situations, aims at becoming socially isolated. Typical social phobias are of speaking, eating, or writing in public, using public laboratories, and attending parties or interviews. One individual may have one social phobia

or many. Corresponding individuals usually fear that other people will det ct and ridicul there phobia.

It has now been found, surprisingly, that substance P antagonists can be employed for the treatment of panic disorder and social phobia. Since the effects which have been found for substance P antagonists in preclinical animal models are analogous to those of phenelzine, fluoxetine, paroxetine and chlordiazepoxide, substance P antagonists can equally be employed clinically for the treatment of panic disorder and social phobia.

This is true in particular of compounds of the formula (I)



and their pharmaceutically utilizable salts, in which

$R_1$ is an unsubstituted or substituted aralkyl, aryloxyalkyl, heteroaralkyl, aroyl, heteroaroyl, cycloalkylcarbonyl, aralkanoyl, heteroarylalkanoyl, aralkoxycarbonyl or arylcarbamoyl radical or the acyl radical of an α-amino acid which is unsubstituted or N-substituted by lower alkanoyl or carbamoyl-lower-alkanoyl;

$R_2$ is cycloalkyl or an unsubstituted or substituted aryl or heteroaryl radical;

$R_3$ is hydrogen, alkyl, carbamoyl or an alkanoyl or alkenoyl radical which is unsubstituted or substituted by carboxyl or esterified or amidated carboxyl;

$R_4$ is an unsubstituted or substituted aryl or unhydrogenated or partially hydrogenated heteroaryl radical;

$X_1$ is methylene, ethylene, a direct linkage, a carbonyl group which may be ketalized, or an unetherified or etherified hydroxymethylene group;

$X_2$ is alkylene, carbonyl or a direct linkage; and

$X_3$ is carbonyl, oxo-lower-alkylene, oxo(aza)-lower-alkylene or an alkylene radical which is unsubstituted or substituted by phenyl, hydroxymethyl, carboxyl which may be esterified or amidated, or by hydroxyl in a position higher than α.

Said aryl, aroyl, aralkanoyl, het roaryl and heteroaroyl radicals can be unsubstituted or substituted, such as mono-, di- or trisubstituted, in particular mono- or disubstituted, for example by aromatically bonded lower alkyl, lower alkoxy, halogen and/or trifluoromethyl. Aryl, aralkyl, aryloxyalkyl, cycloalkylcarbonyl and aroyl radicals are preferably mono- or disubstituted, such as 3-mono- or 3,5-disubstituted, in the stated manner; heteroaryl, heteroaralkyl, heteroaralkanoyl and heteroaroyl radicals are preferably unsubsituted. Aralkyl is, for example, phenyl- or diphenyl-lower-alkyl which is unsubstituted or substituted in the phenyl or naphthyl moiety.

Aryloxy-lower-alkyl is, for example, phenoxy-lower-alkyl which is unsubstituted or substituted in the phenyl moiety.

Heteroaralkyl is, for example, heteroaryl-lower-alkyl having as heteroaryl radical an azaheteroaryl which is a 6-membered monocycle or a bicycle composed of a 6-membered and a 5- or 6-membered ring.

Aroyl is, for example, unsubstituted or substituted benzoyl, such as benzoyl, 3-lower-alkyl-, 3-lower-alkoxy-, 3-halo-, 3-dimethylamino-, 3,5-di-lower-alkyl-, 3,5-di-lower-alkoxy-, 3,5-dihalo- or 3,5-ditrifluoromethylbenzoyl, or secondarily unsubstituted or substituted naphthoyl such as 1- or 2-naphthoyl.

Heteroaroyl is, for example, an azaheteroaryl which is a 6-membered monocycle or a bicycle composed of a 6-membered and a 5- or 6-membered ring, such as pyridylcarbonyl or quinolinylcarbonyl.

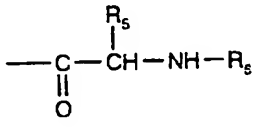
Cycloalkanoyl is, for example, unsubstituted or substituted 3- to 8-, in particular 5- to 7-, membered cycloalkylcarbonyl such as cyclohexylcarbonyl, 3-lower-alkyl-, 3-lower-alkoxy-, 3-halo-, 3-dimethylamino-, 3,5-di-lower-alkyl, 3,5-di-lower-alkoxy-, 3,5-dihalo- or 3,5-ditrifluoromethylcyclohexylcarbonyl.

Aralkanoyl is, for example, phenyl- or diphenyl-lower-alkanoyl which is unsubstituted or substituted in the phenyl moiety.

Heteroarylalkanoyl is, for example, a heteroaryl-lower-alkanoyl having as heteroaryl radical an azaheteroaryl which is a 6-membered monocycle or a bicycle composed of a 6-membered and a 5- or 6-membered ring.

Arylcarbamoyl is, for example, N-phenylcarbamoyl which is unsubstituted or substituted in the phenyl moiety.

Acyl radicals of unsubstituted or N-alkanoylated α-amino acids are derived, in particular, from α-amino acids which occur in nature as building blocks of peptides and are unsubstituted or lower alkanoylated, for example N-$C_2$-$C_7$-alkanoylated, such as substituted by acetyl, propionyl, butyryl or pivaloyl. Examples are groups of the formula



(Ia)

in which $R_5$ is hydrogen or a lower alkyl, such as $C_1$-$C_4$alkyl, a radical which is unsubstituted or substituted by hydroxyl, amino, mercapto, unsubstituted or hydroxyl-substituted phenyl, carboxyl, carbamoyl or ureido, for example methyl, isopropyl, isobutyl, secondary butyl, hydroxymethyl, mercaptomethyl, 2-methylmercaptoethyl, 3-ureidopropyl, 4-aminobutyl, carboxymethyl, carbamoylmethyl, 2-carboxyethyl, 2-carbamoylethyl, benzyl or 4-hydroxybenyl, and $R_6$ is lower alkanoyl, for example $C_2$-$C_7$alkanoyl, such as acetyl, propionyl, butyryl or pivaloyl. However, it can also be the acyl group of a heterocyclic α-amino acid which occurs naturally as a building block of peptides, such as prolyl, tryptophanyl or histidinyl.

Cycloalkyl is, for example, 5- to 7-membered cycloalkyl such as, in particular, cyclohexyl or secondarily cyclopentyl or cycloheptyl.

Aryl is, for example, phenyl or, in particular as $R_4$, naphthyl.

Heteroaryl is, for example, 6-membered monocyclic azaheteroaryl such as pyridyl, or as $R_4$ in particular heteroaryl composed of an unhydrogenated or partially hydrogenated 5- or 6-membered mono- or diaza- or oxaheteroaryl radical and a 6-membered aryl radical, such as

benzofuranyl, for example benzofuran-2-yl or -3-yl, indolyl, for example indol-2-yl or -3-yl, 2,3-dihydroindolyl, for example 2,3-dihydroindol-2-yl or -3-yl, benzimidazolyl, for example benzimidazol-2-yl, quinolyl, for example 4-quinolinyl, isoquinolinyl, for example 1-isoquinolinyl, quinazolinyl, for example 4-quinazolinyl, or 1,2,3,4-tetrahydroquinolinyl, for example 1,2,3,4-tetrahydro-4-quinolinyl.

Heteroaryl-lower-alkanoyl having as heteroaryl radical an azaheteroaryl which is a 6-membered monocycle or a bicycle composed of a 6-membered and a 5- or 6-membered ring is, for example, corresponding heteroaryl-$C_1$-$C_4$alkanoyl, such as 2-pyridyl- or 4-pyridylacetyl, 2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-3-ylcarbonyl.

Alkyl is, in particular, lower alkyl; alkylene in particular lower alkylene.

Ketalized carbonyl groups are, for example, ketalized with an aliphatic alcohol or dialcohol such as with a lower alkanol or a lower alkanediol, and are, for example, di-lower-alkoxymethylene or lower alkylenedioxymethylene.

Etherified hydroxymethylene is etherified in particular with an aliphatic alcohol such as a lower alkanol and is, for example, lower alkoxymethylene.

Carboxyl which may be esterified or amidated is, for example, carboxyl, lower alkoxycarbonyl, carbamoyl or N-mono- or N,N-di-lower-alkylcarbamoyl.

Alkanoyl or alkenoyl radicals which are unsubstituted or substituted by carboxyl or esterified or amidated carboxyl are, for example, lower alkanoyl such as $C_2$-$C_7$alkanoyl, such as acetyl, propionyl, butyryl or pivaloyl, carboxy-lower-alkanoyl, such as carboxy-$C_3$-$C_7$alkanoyl, such as succinoyl, glutaroyl or adipoyl, or carboxy-lower-alkenoyl, such as carboxy-$C_3$-$C_5$-alkenoyl, such as maleyl, fumaroyl or tartroyl, in which carboxyl can also be esterified or amidated, and is, for example, lower alkoxycarbonyl such as $C_1$-$C_4$alkoxycarbonyl, for example methoxy- or ethoxycarbonyl, carbamoyl or N-mono- or N,N-di-lower-alkylcarbamoyl, such as N-mono- or N,N-di-$C_1$-$C_4$alkylcarbamoyl, for example N-methyl- or N,N-dimethylcarbamoyl.

Lower alkylene substituted by hydroxyl in a position higher than α is, for example, hydroxylated in position 2 to the N atom.

Lower alkylene substituted by hydroxymethyl or carboxyl which may be esterified or amidated is, for example, substituted in position 1, 2 or, if present, 3 to the N atom by carboxyl, lower alkoxycarbonyl, carbamoyl, N-mono- or N,N-di-lower-alkylcarbamoyl or hydroxymethyl.

Lower radicals and compounds are to be anderstood to mean hereinbefore and hereinafter for example those which have up to and including 7, preferably up to and including 4, carbon atoms (C atoms).

Lower alkyl is, for example, $C_1$-$C_7$alkyl, preferably $C_1$-$C_4$alkyl, such as, in particular, methyl or secondarily ethyl, propyl, isopropyl or butyl, but can also be isobutyl, secondary butyl, tertiary butyl or a $C_5$-$C_7$alkyl such as pentyl, hexyl or heptyl group.

Lower alkylene is, for example, $C_1$-$C_7$alkylene, preferably $C_1$-$C_4$alkylene, such as methylene, ethylene, 1,3-propylene, 1,4-butylene or 1,5-pentylene.

Phenyl- or diphenyl-lower-alkyl which is unsubstituted or substituted in the phenyl is, for example, corresponding phenyl or diphenyl-$C_1$-$C_4$alkyl, such as benzyl, 2,4-dichlorobenzyl, 3,5-ditrifluoromethylbenzyl, 2-phenylethyl or 2,2-diphenylethyl.

The phenyl- or diphenyl-lower-alkanoyl which is unsubstituted or substituted in the phenyl moiety is, for example, corresponding phenyl- or diphenyl-$C_1$-$C_4$alkanoyl, such as 2,2-diphenylacetyl or 2,3-diphenylpropionyl.

Phenoxy-lower-alkyl which is unsubstituted or substituted in the phenyl is, for example, phenoxy-$C_1$-$C_4$alkyl substituted by halogen and/or triazolyl, such as 2-[2-(1H-1,2,4-triazol-1-yl)-4-chlorophenoxy]ethyl.

Heteroaryl-lower-alkyl having as heteroaryl radical an azaheteroaryl which is a 6-membered monocycle or a bicycle composed of a 6-membered and 5- or 6-membered ring is, for example, pyridyl- or quinolinyl-$C_1$-$C_4$alkyl, such as 4-quinolinylmethyl.

Lower alkoxy is, for example, $C_1$-$C_7$alkoxy, preferably $C_1$-$C_4$alkoxy, such as methoxy, ethoxy, propyloxy, isopropyloxy or butyloxy, but can also be iobutyloxy, secondary butyloxy, tertiary butyloxy or a pentyloxy, hexyloxy or heptyloxy group.

Halogen is, for example, halogen of atomic number up to and including 35 such as chlorine or fluorine, also bromine.

Lower alkoxycarbonyl is, for example, $C_1$-$C_7$alkoxycarbonyl, preferably $C_1$-$C_4$alkoxycarbonyl, such as methoxycarbonyl, ethoxycarbonyl, propyloxycarbonyl, isopropyloxycarbonyl or butyloxycarbonyl, but can also be isobutyloxycarbonyl, secondary butyloxycarbonyl, tertiary butyloxycarbonyl or a pentyloxycarbonyl, hexyloxycarbonyl or heptyloxycarbonyl group.

N-Lower-alkylcarbamoyl is, for example, N-$C_1$-$C_7$alkylcarbamoyl, preferably N-$C_1$-$C_4$alkyl-carbamoyl, such as methylcarbamoyl, ethylcarbamoyl, propylcarbamoyl, isopropylcarbamoyl or butylcarbamoyl, but can also be isobutylcarbamoyl, secondary butylcarbamoyl, tertiary butylcarbamoyl or a pentylcarbamoyl, hexylcarbamoyl or heptylcarbamoyl group.

N,N-Di-lower-alkylcarbamoyl is, for example, N,N-di-$C_1$-$C_7$alkylcarbamoyl, preferably N,N-di-$C_1$-$C_4$alkylcarbamoyl, such as N,N-dimethylcarbamoyl, N,N-diethylcarbamoyl, N-ethyl-N-methylcarbamoyl, N,N-dipropylcarbamoyl, N-methyl-N-propylcarbamoyl, N-isopropyl-N-methylcarbamoyl or N-butyl-N-methylcarbamoyl, but can also be N-isobutyl-N-methyl-carbamoyl, N-methyl-N-secondary-butylcarbamoyl, N-methyl-N-tertiary-butylcarbamoyl or an N-methyl-N-pentylcarbamoyl, N-hexyl-N-methylcarbamoyl or N-heptyl-N-methylcarbamoyl group.

Lower alkylene substituted by hydroxyl in a position higher than $\alpha$ and lower than $\omega$ is, for example, 1,3-(2-hydroxy)propylene, 1,4-(2-hydroxy)butylene, 1,4-(3-hydroxy)butylene, 1,5-(2-hydroxy)pentylene, 1,5-(3-hydroxy)pentylene or 1,5-(4-hydroxy)pentylene.

Carboxyl-substituted lower alkylene is, for example, carboxymethylene, 1- or 2-carboxy-ethylene, 1,3-(2-carboxy)propylene, 1,4-(2-carboxy)butylene, 1,4-(3-carboxy)butylene, 1,5-(2-carboxy)pentylene, 1,5-(3-carboxy)pentylene or 1,5-(4-carboxy)pentylene.

Lower alkylene substituted by lower alkoxycarbonyl is, for example, lower alkoxycarbonylmethylene, 1- or 2-lower-alkoxycarbonylethylene, 1,3-(2-lower-alkoxycarbonyl)propylene, 1,4-(2-lower-alkoxycarbonyl)butylene, 1,4-(3-lower-alkoxycarbonyl)butylene, 1,5-(2-lower-alkoxycarbonyl)pentylene, 1,5-(3-lower-alkoxycarbonyl)pentylene or 1,5-(4-lower-alkoxycarbonyl)pentylene, where lower alkoxycarbonyl is, in each case, for example $C_1$-$C_4$alkoxycarbonyl, such as methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl or butoxycarbonyl.

Lower alkylene substituted by carbamoyl, N-mono- or N,N-di-lower-alkylcarbamoyl is, in particular, substituted by carbamoyl and is, for example, carbamoylmethylene, 1- or 2-carbamoylethylene, 1,3-(2-carbamoyl)propylene, 1,4-(2-carbamoyl)butylene, 1,4-(3-carbamoyl)butylene, 1,5-(2-carbamoyl)pentylene, 1,5-(3-carbamoyl)pentylene or 1,5-(4-carbamoyl)pentylene.

Lower alkylene substituted by hydroxymethyl is, for example, 2-hydroxyethylidene, 2,3-(1-hydroxy)propylene, 1,3-(2-hydroxymethyl)propylene, 2,4-(1-hydroxy)butylene, 1,4-(2-hydroxymethyl)butylene, 1,4-(3-hydroxymethyl)butylene, 1,5-(2-hydroxymethyl)-pentylene, 1,5-(3-hydroxymethyl)pentylene or 1,5-(4-hydroxymethyl)pentylene.

Lower alkoxymethylene is, for example, $C_1$-$C_4$alkoxymethylene such as methoxymethylene, ethoxymethylene, propyloxymethylene or butyloxymethylene.

Di-lower-alkoxymethylene is, for example, di-$C_1$-$C_4$alkoxymethylene, such as dimethoxymethylene, diethoxymethylene, dipropyloxymethylene or dibutyloxymethylene.

Lower alkylenedioxymethylene is, for example, 5- to 8-membered, in particular 5- or 6-membered, 1,3-dioxa-2-cycloalkyl, such as 1,3-dioxa-2-cyclobutyl, 1,3-dioxa-2-cyclopentyl (1,3-dioxolan-2-yl), 1,3-dioxa-2-cyclohexyl (1,3-dioxan-2-yl) or 1,3-dioxa-2-cycloheptyl.

Compounds of the formula (I) have basic or, if $R_3$ and/or $X_3$ is substituted by carboxyl, amphoteric characteristics and are accordingly able to form acid addition salts and, where appropriate, internal salts.

Acid addition salts of compounds of the formula (I) are, for example, their pharmaceutically utilizable salts with suitable mineral acids such as hydrohalic acids, sulfuric acid or phosphoric acid, for example hydrochlorides, hydrobromides, sulfates, bisulfates or phosphates, or salts with suitable aliphatic or aromatic sulfonic acids or N-substituted sulfamic acids, for example methanesulfonates, benzenesulfonates, p-toluenesulfonates or N-cyclohexylsulfamates (cyclamates).

Only the pharmaceutically utilizable non-toxic salts are used in therapy.

The above compounds and their preparation are described, for example, in European Patent Application having the publication no. 532,456 (EP 532,456).

The novel action of the compounds of the formula (I) and their salts can be established, for example, in the following design of tests: adult male rats, referred to as residents, and young preadult rats, referred to as intruders, are put together in the cage which is home to the adult rats. The activity of the intruder with regard to the resident, which is manifested by sniffing, anogenital inspection, nose contact, licking and playing together, is recorded manually and recorded cumulatively over a period of 5 minutes. In this design of tests, phenelzine, fluoxetine, paroxetine and chlordiazepoxide are active in the submilligram and low milligram range since they lead to a significant intensification and increase in social behaviour; all these substances are employed as effective therapeutic treatment of panic disorder in humans. The dose range in which a distinct activity is to be observed in this test on rats is estimated to be a range from about 0.1 to about 10 mg/kg orally.

The results of analogous experiments with a compound of the formula (I) or a salt thereof reveals a qualitatively and quantitatively comparable increase in the time spent by the intruder investigating the resident (MED in the submilligram range). The conclusion which emerges from these tests is that administration of compounds of the formula (I) or a salt thereof leads, through inhibition of the panic behaviour which is actually to be expected, to a significant intensification of the social behaviour in the test animals. Accordingly, exactly like phenelzine, fluoxetine and paroxetine, the compounds of the formula (I) and their salts can be employed for the treatment of panic disorder and social phobia.

The use of compounds of formula (I) and pharmaceutically acceptable salts thereof can be established in clinical trials, e.g. as described as follows: The compounds to be used for the treatment of social phobia are administered to patients who have primary DSM-III-R diagnosis of social phobia, e.g. diagnosed by using the Structured Clinical Interview for DSM-III-R, e.g. in a 12 week open clinical trial. The treatment begins e.g. using 10 mg of a Substance P receptor antagonist daily and may be increased according to clinical response and side effects. Patients complete theirself-report measures at baseline and at e.g. weeks 4, 8, and 12. These measures include the fear of negative evaluation scale, social avoidance and distress scale, the social anxiety thoughts questionnaire, the fear questionnaire, the state-trait anxiety inventory, the Beck depression inventory, the social adjustment scale self-report, and the Sheehan disability scale. The responders e.g. at endpoint rate on the clinical global impression change by defining moderately or marketly improved.

The invention therefore primarily relates to the use of a substance P antagonist, in particular one of the compounds of the formula (I) defined hereinbefore and hereinafter, or a pharmaceutically utilizable salt thereof, for the production of pharmaceutical products for the treatment of panic disorder and social phobia.

The invention furthermore relates to a method for the treatment of panic disorder and social phobia, wherein a therapeutically effective amount of a substance P antagonist, in particular one of the compounds of the formula (I) defined hereinbefore or hereinafter, or a pharmaceutically utilizable salt thereof, is administered to a warm-blooded animal including man in need.

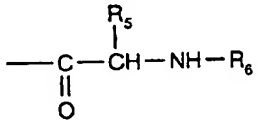
The invention likewise relates to pharmaceutical products for the treatment of panic disorder and social phobia, which comprise a substance P antagonist, in particular one of the compounds of the formula (I) defined hereinbefore and hereinafter, or a pharmaceutically utilizable salt thereof, with or without auxiliaries and additives.

The invention furthermore relates to the use of a substance P antagonist, in particular one of the compounds of the formula (I) defined hereinbefore and hereinafter, or a salt thereof, for the treatment of panic disorder and social phobia.

The invention primarily relates to the corresponding use of a compound of the formula (I) or of a pharmaceutically utilizable salt thereof, in which $R_1$ is a phenyl-, diphenyl-, naphthyl- or fluorenyl-lower-alkyl radical which is unsubstituted or substituted in the phenyl moiety by lower alkyl, lower alkoxy, di-lower-alkylamino, halogen and/or trifluoromethyl, or a phenoxy-lower-alkyl radical which is unsubstituted or substituted in the phenyl moiety by halogen and/or triazolyl, or a heteroaryl-lower-alkyl radical which has as heteroaryl radical an azaheteroaryl which is a 6-membered monocycle or a bicycle composed of a 6-membered and a 5- or 6-membered ring, or a benzoyl, naphthoyl, fluorenoyl or 3- to 8-membered cycloalkylcarbonyl radical which is unsubstituted or substituted by lower alkyl, lower alkoxy, hydroxyl, di-lower-alkylamino, halogen, cyano and/or trifluoromethyl, or a phenyl- or diphenyl-lower-alkanoyl radical which is unsubstituted or substituted in the phenyl moiety by lower alkyl, lower alkoxy, di-lower-alkylamino, halogen and/or trifluoromethyl, or a heteoaryl-lower-alkanoyl radical which has as heteroaryl radical an azaheteroaryl which is a 6-membered monocycle or a bi- or tricycle composed of a 6-membered and one or two 5- or 6-membered ring(s), or a phenyl-lower-alkoxycarbonyl or N-phenylcarbamoyl radical which is unsubstituted or substituted in the phenyl moiety by lower alkyl, lower alkoxy, di-lower-alkylamino or halogen and/or trifluoromethyl, or the acyl radical of an α-amino acid which is unsubstituted or N-substituted by lower alkanoyl or carbamoyl-lower-alkanoyl and occurs in nature as building block of peptides, $R_2$ is 5- to 7-membered cycloalkyl or a phenyl, naphthyl or 6-membered monocyclic azaheteroaryl radical which is unsubstituted or substituted by aromatically bonded lower alkyl, lower alkoxy, halogen and/or trifluoromethyl, $R_3$ is hydrogen, lower alkyl, carbamoyl, lower alkanoyl, carboxy-lower-alkanoyl or carboxy-lower-alkenoyl, lower alkoxycarbonyl-lower-alkyl, carbamoyl-lower-alkanoyl, N-mono- or N,N-di-lower-alkylcarbamoyl-lower-alkanoyl, N-cycloalkylcarbamoyl-lower-alkanoyl or N-phenyl-carbamoyl-lower-alkanoyl $R_4$ is a phenyl, naphthyl or pyridyl radical which is unsubstituted or substituted by lower alkyl, lower alkoxy, halogen and/or trifluoromethyl, or a heteroaryl radical which is unsubstituted or C-substituted by lower alkyl, lower alkoxy, halogen and/or trifluoromethyl and possibly N-substituted by lower alkanoyl and is composed of an unhydrogenated or partially hydrogenated 5- or 6-membered mono- or diaza- or oxaheteroaryl radical and a 6-membered aryl radical, $X_1$ is methylene, ethylene, a carbonyl group which may be ketalized by a lower alkanol or a lower alkanediol, or a hydroxymethylene group which is unetherified or etherified with a lower alkanol, or a direct linkage, $X_2$ is carbonyl, lower alkylene or a direct linkage, and $X_3$ is carbonyl, oxo-lower-

alkylene, oxo(aza)-lower-alkylene or a lower alkylene radical which is unsubstituted or substituted by phenyl or in position 1, 2 or, if present, 3 to the N atom by carboxyl, lower alkoxycarbonyl, carbamoyl, N-mono or N,N-di-lower-alkylcarbamoyl or hydroxymethyl, and to pharmaceutical products containing corresponding compounds.

The invention primarily relates to the corresponding use of a compound of the formula (I) or of a pharmaceutically utilizable salt thereof, in which $R_1$ is phenyl- or diphenyl-$C_1$-$C_4$alkyl, which is unsubstituted or substituted in the phenyl moiety by lower alkyl, lower alkoxy, di-lower-alkylamino, halogen and/or trifluoromethyl, such as benzyl, 2,4-dichlorobenzyl, 3,5-ditrifluoromethylbenzyl, 2-phenylethyl or 2,2-diphenylethyl, or phenoxy-$C_1$-$C_4$alkyl, pyridyl- or quinolinyl-$C_1$-$C_4$alkyl, which is unsubstituted or substituted in the phenyl by halogen and/or triazolyl, such as 4-quinolinylmethyl, or benzoyl which is unsubstituted or substituted by lower alkyl, lower alkoxy, di-lower-alkylamino, halogen and/or trifluoromethyl, such as benzoyl, 3-lower-alkyl-, 3-lower-alkoxy-, 3-halo-, 3-dimethylamino-, 3,5-di-lower-alkyl-, 3,5-di-lower-alkoxy-, 3,5-dihalo- or 3,5-ditrifluoromethylbenzoyl, or secondarily naphthoyl which is unsubstituted or substituted by lower alkyl, lower alkoxy, di-lower-alkylamino, halogen and/or trifluoromethyl, such as 1- or 2-naphthoyl, or pyridylcarbonyl or quinolinylcarbonyl which is unsubstituted or substituted by lower alkyl, lower alkoxy, halogen and/or trifluoromethyl, or 5- to 7-membered cycloalkylcarbonyl which is unsubstituted or substituted by lower alkyl, lower akoxy, di-lower-alkylamino, halogen and/or trifluoromethyl, such as cyclohexylcarbonyl, 3-methyl-, 3-methoxy-, 3-chloro-, 3-dimethylamino-, 3,5-dimethyl-, 3,5-dimethoxy-, 3,5-dichloro- or 3,5-ditrifluoromethylcyclohexylcarbonyl, or phenyl- or diphenyl-$C_1$-$C_4$alkanoyl which is unsubstituted or substituted in the phenyl by lower alkyl, lower alkoxy, di-lower-alkylamino, halogen and/or trifluoromethyl, such as 2,2-diphenylacetyl or 2,3-diphenylpropionyl, or N-phenylcarbamoyl which is unsubstituted or substituted in the phenyl moiety by lower alkyl, lower alkoxy, di-lower-alkylamino, halogen and/or trifluoromethyl, or a group of the formula (Ia)



(Ia)

in which $R_5$ is hydrogen, $C_1$-$C_4$alkyl which is unsubstituted or substituted by hydroxyl, mercapto, amino, unsubstituted or hydroxy-substituted phenyl, carboxyl, carbamoyl or

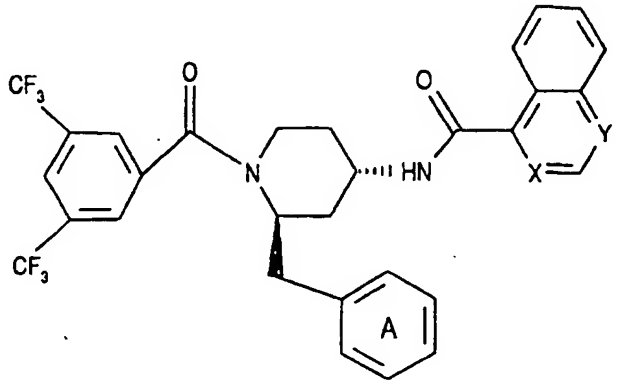
ureido, and $R_6$ is $C_2$-$C_7$alkanoyl, $R_2$ is 5- to 7-memebered cycloalkyl or a phenyl, naphthyl or pyridyl radical which is unsubstituted or substituted by $C_1$-$C_4$alkyl, $C_1$-$C_4$alkoxy, halogen and/or trifluoromethyl, $R_3$ is hydrogen, $C_1$-$C_7$alkyl, carbamoyl, $C_2$-$C_7$alkanoyl, carboxy-$C_1$-$C_4$alkanoyl or carboxy-$C_2$-$C_4$alkenoyl, $R_4$ is phenyl or naphthyl which is unsubstituted or substituted by $C_1$-$C_4$alkyl, $C_1$-$C_4$alkoxy, halogen and/or trifluoromethyl, or unsubstituted pyridyl, benzofuranyl, indolyl, 2,3-dihydroindolyl, benzimidazolyl, quinolyl or 1,2,3,4-tetrahydroquinolinyl, $X_1$ is methylene, hydroxymethylene, $C_1$-$C_4$alkoxymethylene, carbonyl or di-$C_1$-$C_4$-alkoxymethylene or a direct linkage, $X_2$ is $C_1$-$C_7$alkylene, carbonyl or a direct linkage, and $X_3$ is carbonyl, $C_1$-$C_4$alkylene, carboxy-$C_1$-$C_4$alkylene, $C_1$-$C_4$alkoxycarbonyl-$C_1$-$C_4$-alkylene, carbamoyl-$C_1$-$C_4$alkylene or hydroxymethyl-$C_1$-$C_4$alkylene, and to pharmaceutical products comprising corresponding compounds.

The invention primarily relates to the corresponding use of a compound of the formula (I) or of a pharmaceutically utilizable salt thereof, in which $R_1$ is benzoyl, naphthoyl or phenyl-$C_1$.$C_4$alkanoyl which is unsubstituted or substituted by $C_1$-$C_4$alkyl such as methyl, $C_1$.$C_4$alkoxy such as methoxy, halogen and/or trifluoromethyl, or unsubstituted pyridylcarbonyl or quinolinylcarbonyl, or a group of the formula (Ia) in which $R_5$ is hydrogen, $C_1$-$C_4$alkyl which is unsubstituted or substituted by hydroxyl, mercapto, amino, unsubstituted or hydroxyl-substituted phenyl, carboxyl, carbamoyl or ureido, for example methyl, isopropyl, isobutyl, secondary butyl, hydroxymethyl, mercaptomethyl, 2-methylmercaptoethyl, 3-ureidopropyl, 4-aminobutyl, carboxymethyl, carbamoylmethyl, 2-carboxyethyl, 2-carbamoylethyl, benzyl or 4-hydroxybenzyl, and $R_6$ is $C_2$-$C_7$alkanoyl such as acetyl, propionyl, butyryl or pivaloyl, $R_2$ is 5- to 7-membered cycloalkyl, in particular cyclohexyl, or secondarily cyclopentyl or cycloheptyl, or a phenyl, naphthyl or pyridyl radical which is unsubstituted or substituted by $C_1$-$C_4$alkyl such as methyl, $C_1$-$C_4$alkoxy such as methoxy, halogen and/or trifluoromethyl, $R_3$ is hydrogen, $C_1$-$C_7$alkyl such as methyl, ethyl, propyl, isopropyl or butyl, isobutyl, secondary butyl or tertiary butyl, carbamoyl, $C_2$-$C_7$alkanoyl such as acetyl, propionyl, butyryl or pivaloyl, carboxy-$C_1$-$C_4$alkanoyl such as succinoyl, glutaroyl or adipoyl, or carboxy-$C_3$-$C_5$alkenoyl such as maleyl, fumaroyl or tartroyl, $R_4$ is phenyl or naphthyl which is unsubstituted or substituted by $C_1$-$C_4$alkyl such as methyl, $C_1$-$C_4$alkoxy such as methoxy, halogen and/or trifluoromethyl, or unsubstituted pyridyl, benzofuranyl, indolyl, benzimidazolyl or quinolyl, $X_1$ is methylene, hydroxymethylene, $C_1$-$C_4$alkoxymethylene such as methoxymethylene, ethoxymethylene, propyloxymethylene or butyloxymethylene, carbonyl, di-$C_1$-$C_4$alkoxymethylene such as dimethoxymethylene,

diethoxymethylene, dipropyloxymethylene or dibutyloxymethylene, or a direct linkage, $X_2$ is $C_1$-$C_7$alkylene such as methylene or secondarily ethylene or 1,3-propylene, carbonyl or a direct linkage, and $X_3$ is carbonyl, $C_1$-$C_4$alkylene such as methylene, ethylene or 1,3-propylene, carboxy-$C_1$-$C_4$alkylene such as 1,3-(2-carboxy)propylene, 1,4-(2-carboxy)-butylene, 1,4-(3-carboxy)butylene, $C_1$-$C_4$alkoxycarbonyl-$C_1$-$C_4$-alkylene such as 1,3-(2-$C_1$-$C_4$alkoxycarbonyl)propylene, 1,4-(2-$C_1$-$C_4$alkoxycarbonyl)butylene, 1,4-(3-$C_1$-$C_4$-alkoxycarbonyl)butylene, 1,5-(2-$C_1$-$C_4$alkoxycarbonyl)pentylene, 1,5-(3-$C_1$-$C_4$alkoxy-carbonyl)pentylene or 1,5-(4-$C_1$-$C_4$alkoxycarbonyl)pentylene, where $C_1$-$C_4$alkoxycarbonyl is, in each case, for example methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl or butoxycarbonyl, or carbamoyl-$C_1$-$C_4$alkylene such as 1,3-(2-carbamoyl)propylene, 1,4-(2-carbamoyl)butylene, 1,4-(3-carbamoyl)butylene, 1,5-(2-carbamoyl)pentylene, 1,5-(3-carbamoyl)pentylene or 1,5-(4-carbamoyl)pentylene or hydroxymethyl-$C_1$-$C_4$alkylene, such as 1,3-(2-hydroxymethyl)propylene, 1,4-(2-hydroxymethyl)butylene, 1,4-(3-hydroxy-methyl)butylene, 1,5-(2-hydroxymethyl)pentylene, 1,5-(3-hydroxymethyl)pentylene or 1,5-(4-hydroxymethyl)pentylene, and to pharmaceutical products comprising corresponding compounds.

The invention relates above all to the corresponding use of a compound of the formula (I) or of a pharmaceutically utilizable salt thereof, in which $R_1$ is benzoyl which is unsubstituted or mono- or disubstituted by $C_1$-$C_4$alkyl such as methyl, $C_1$-$C_4$alkoxy such as methoxy, halogen of atomic number up to and including 35, such as chlorine, and/or trifluoromethyl, or unsubstituted naphthoyl or phenyl-$C_1$-$C_4$alkanoyl, $R_2$ is phenyl which is unsubstituted or mono- or disubstituted by $C_1$-$C_4$alkyl such as methyl, $C_1$-$C_4$alkoxy such as methoxy, halogen of atomic number up to and including 35, such as chlorine and/or trifluoromethyl, or unsubstituted pyridyl, $R_3$ is hydrogen, $C_1$-$C_4$alkyl such as methyl, ethyl, propyl or isopropyl, carbamoyl or $C_2$-$C_7$alkanoyl such as acetyl, propionyl, butyryl or pivaloyl, $R_4$ is phenyl which is unsubstituted or mono- or disubstituted by $C_1$-$C_4$alkyl such as methyl, $C_1$-$C_4$alkoxy such as methoxy, halogen of atomic number up to and including 35, such as chlorine and/or trifluoromethyl, or unsubstituted naphthyl, pyridyl, benzofuranyl, indolyl, benzimidazolyl or quinolyl, $X_1$ is methylene, hydroxymethylene, carbonyl or a direct linkage, $X_2$ is a direct linkage, and $X_3$ is $C_1$-$C_4$alkylene such as methylene or secondarily ethylene or 1,3-propylene, and to pharmaceutical products comprising corresponding compounds.

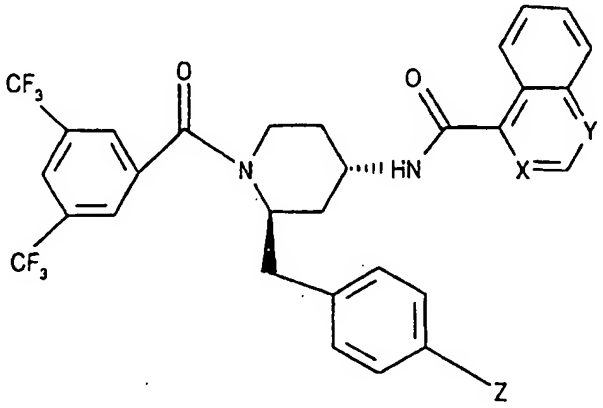
The invention relat s above all to the corresponding use of a compound of the formula (Ib) or of a pharmaceutically utilizable salt thereof




(Ib),

in which X and Y are, independently of one another, N and/or CH, and ring A is unsubstituted or substituted one or more times by substituents selected from the group consisting of lower alkyl, lower alkoxy, halogen, nitro and trifluoromethyl; and to pharmaceutical products comprising corresponding compounds.

The invention relates above all to the corresponding use of a compound of the formula (Ic)




(Ic),

or of a pharmaceutically utilizable salt thereof, in which X is N or CH and Y is N; and Z is halogen such as chlorine; and to pharmaceutical products comprising corresponding compounds.

The invention relates above all to the corresponding use of a compound of the formula (Ic) in which X is N or CH and Y is N; and Z is halogen such as chlorine; and to pharmaceutical products comprising corresponding compounds.

The invention relates above all to the corresponding use of a compound of the formula (I) or of a pharmaceutically utilizable salt thereof, in which $R_1$ is benzoyl which is unsubstituted or mono- or disubstituted by $C_1$-$C_4$alkyl such as methyl, $C_1$-$C_4$alkoxy such as methoxy, halogen of atomic number up to and including 35, such as chlorine, and/or trifluoromethyl, or unsubstituted naphthoyl, $R_2$ is phenyl which is unsubstituted or mono- or disubstituted by halogen of atomic number up to and including 35, such as chlorine, and/or trifluoromethyl, $R_3$ is hydrogen, $R_4$ is unsubstituted quinolyl, $X_1$ is methylene, $X_2$ is a direct linkage, and $X_3$ is $C_1$-$C_4$alkylene such as methylene or secondarily ethylene or 1,3-propylene, and to pharmaceutical products comprising corresponding compounds.

The invention relates above all to the corresponding use of a compound of the formula (I) or of a pharmaceutically utilizable salt thereof selected from the group consisting of:
(2R*,4S*)-2-Benzyl-1-(2-naphthoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3-trifluoromethylbenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-bis-(trifluoromethyl)-benzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(1-naphthoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(2-quinolinoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(4-chloro-phenylacetyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(benzyloxycarbonyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(2-phenylethyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(2-naphthylacetyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(4-quinolylmethyl)-N-(4-quinolylmethyl)-4-piperidineamine or
a salt thereof.

(2R*,4S*)-2-Benzyl-1-(2,4-dichlorobenzyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(2,2-diphenylethyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(phenylcarbamoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(diphenylacetyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(2-pyridylacetyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(4-pyridylacetyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(2,3-diphenylpropionyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-((3S)-(2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-3-yl)-carbonyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3-methoxybenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3-N,N-dimethylaminobenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(cis,cis-3,5-dimethylcyclohexylcarbonyl)-N-(4-quinolyl-methyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-bis-(trifluoromethyl)benzyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2S*,4R*)-2-Benzyl-1-(2-(5-chloro-(1H-1,2,4-triazol-1-yl)phenoxy)ethyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-((S)-phenylalanyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-((R)-phenylalanyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-((S)-N-acetylphenylalanyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-((R)-N-acetylphenylalanyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-((S)-N-(4-carbamoylbutyryl)phenylalanyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-((R)-N-(4-carbamoylbutyryl)phenylalanyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-benzoyl-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3-chlorobenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(4-quinolylmethyl)-N-(3-carbamoyl-propionyl)-4-piperidineamine;

(2R,4S)- or (2R,4R)-2-B nzyl-1-(3,5-dimethylbenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2S,4R) and (2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-phenethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-quinolylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-quinolylmethyl)-4-piperidineamine;
(2R/4S)- or (2R/4R)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-benzyl-4-piperidineamine;
(2S/4R)- or (2S/4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-benzyl-4-piperidineamine;
(2R/4S)- or (2R/4R)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-pyridylmethyl)-4-piperidineamine;
(2R/4S)- or (2R/4R)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-pyridylmethyl)-4-piperidineamine;
(2S,4R)- and (2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-benzyl-N-carbamoyl-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-phenylpropyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-phenylpropyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-methoxybenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-methoxybenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2-methoxyphenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2-methoxyphenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2-methoxyphenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2-methoxyphenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-trifluoromethylbenzyl)-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-trifluoromethylbenzyl)-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2-trifluoromethylphenyl)ethyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2-trifluoromethylphenyl)ethyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2-trifluoromethylphenyl)propyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2-trifluoromethylphenyl)propyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-trifluoromethylbenzyl)-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-trifluoromethylbenzyl)-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(3-trifluoromethylphenyl)ethyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(3-trifluoromethylphenyl)ethyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(3-trifluoromethylphenyl)propyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(3-trifluoromethylphenyl)propyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-trifluoromethylbenzyl)-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-trifluoromethylbenzyl)-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(4-trifluoromethylphenyl)ethyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(4-trifluoromethylphenyl)ethyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(4-trifluoromethylphenyl)propyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(4-trifluoromethylphenyl)propyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,3-dimethoxybenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,3-dimethoxybenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,3-dimethoxyphenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,3-dimethoxyphenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,3-dimethoxyphenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,3-dimethoxyphenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,4-dimethoxybenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,4-dimethoxybenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,4-dimethoxyphenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,4-dimethoxyphenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,4-dimethoxyphenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,4-dimethoxyphenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,5-dimethoxybenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,5-dimethoxybenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,5-dimethoxyphenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,5-dimethoxyphenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,5-dimethoxyphenyl)propyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,5-dimethoxyphenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,6-dimethoxybenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,6-dimethoxybenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,6-dimethoxyphenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,6-dimethoxyphenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,6-dimethoxyphenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,6-dimethoxyphenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,3-methylenedioxybenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,3-methylenedioxybenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,3-methylenedioxyphenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,3-methylenedioxyphenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,3-methylenedioxyphenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,3-methylenedioxyphenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,4-methylenedioxybenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,4-methylenedioxybenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,4-methylenedioxyphenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,4-methylenedioxyphenyl)ethyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,4-methylenedioxyphenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,4-methylenedioxyphenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-indolylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-quinolinylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-quinolinylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-chlorobenzyl)-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-methoxy-1-naphthylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-methoxy-1-naphthylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-indolylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-quinolinylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-quinolinylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-quinolinylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-quinolinylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-methoxy-1-naphthylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-methoxy-1-naphthylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-indolylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;
(2S;4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-quinolinylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-quinolinylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-quinolinylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-methoxy-1-naphthylmethyl)-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-methoxy-1-naphthylmethyl)-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(2-indolylmethyl)-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(2-indolylmethyl)-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(2-quinolinylmethyl)-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(2-quinolinylmethyl)-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(3-quinolinylmethyl)-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(3-quinolinylmethyl)-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(2-chlorobenzyl)-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(2-chlorobenzyl)-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(3-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(3-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(4-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(4-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(4-methoxy-1-naphthyl-methyl)-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(4-methoxy-1-naphthyl-methyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(2-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(2-indolylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(2-quinolinylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(2-quinolinylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3-quinolinylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3-quinolinylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(2-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(2-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(4-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(4-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(4-methoxy-1-naphthylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(4-methoxy-1-naphthylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(2-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(2-indolylmethyl)-4--piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(3-indolylmethyl)-4--piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(2-quinolinylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(2-quinolinylmethyl)-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(3-quinolinylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(3-quinolinylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(2-chlorobenzyl)-4--piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(2-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(3-chlorobenzyl)-4--piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(3-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(4-chlorobenzyl)-4--piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(4-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(4-methoxy-1-naphthylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(4-methoxy-1-naphthylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;
(2R,4S) and (2R,4R)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-phenethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-bis-(trifluoromethyl)-benzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(2,4-dichlorobenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(phenylacetyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(2,6-dichlorobenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dibromobenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(9-fluorenoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3-toluoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3-bromobenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dihydroxybenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3-cyanobenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(2-chlorobenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(4-chlorobenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(9-fluorenyl)-N-(4-quinolylmethyl)-4-piperidineamine;

(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(4-quinolylmethyl)-N-methyl-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(4-quinolylmethyl)-N-cyclohexyl-carbamoyl-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(4-quinolylmethyl)-N-phenylcarbamoyl-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(2-phenylethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-bis-(trifluoromethyl)-benzoyl)-N-(2-phenylethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(2-naphthoyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3,5-dimethylbenzoyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(4-quinolylcarbonyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3-indolylcarbonyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(2-indolylcarbonyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(5-methoxy-2-indolylcarbonyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(1-naphthoyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(phenylacetyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(2-methoxybenzyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(N-acetyl-3-indolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(2-benzo[b]furanylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3-methyl-2-benzo[b]thiophenyl-methyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(5-methoxy-3-indolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;

(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-phenylcarbamoyl-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-diphenylmethyl-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3,4-dihydro-2H-1-benzopyran-2-carbonyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(4-methoxybenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*,1'R*)-N-Benzyl-1-(3,5-dimethylbenzoyl)-2-(1'-hydroxy-1'-phenylmethyl)-4-piperidineamine;
(2R*,4S*,1'R*)-2-(1'-hydroxy-1'-phenylmethyl)-1-(3,5-dimethylbenzoyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*,1'S*)-1-(3,5-Dimethylbenzoyl)-2-(1'-hydroxy-1'-phenylmethyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*,1'R*)-2-{1'-Hydroxy-1'-(4-chlorophenyl)methyl}-1-(3,5-dimethylbenzoyl)--N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*,1'S*)-1-(3,5-Dimethylbenzoyl)-2-{1'-hydroxy-1'-(4-chlorophenyl)-methyl}-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*,1'S*)-1-(3,5-Dimethylbenzoyl)-2-{1'-hydroxy-1'-(3,4-dichlorophenyl)--methyl}-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-N-Benzyl-1-(3,5-dimethylbenzoyl)-2-benzoyl-4-piperidineamine;
(2R*,4S*)-2-(4-Chlorobenzyl)-1-(3,5-dimethylbenzoyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-2-(3,4-Dichlorobenzyl)-1-(3,5-dimethylbenzoyl)-N-(4-quinolinylmethyl)--4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-phenyl-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dichlorobenzoyl)-2-phenyl-N-(4-quinolinmethyl)-4-piperidineamine;
(2R*,4S*)-1-(1-Naphthoyl)-2-phenyl-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(1-naphthyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(2-naphthyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(4-methoxyphenylmethyl)-N-(4-quinolinyl-methyl)-4-piperidineamine;

(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(3-methoxyphenylmethyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(4-nitrobenzyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(4-trifluoromethylphenylmethyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(2,4-dichlorophenylmethyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(2-phenylethyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(2-phenylethenyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-benzoyl-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(4-chlorobenzoyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(2-naphthyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(4-methoxybenzyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(3-methoxybenzyl)-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(4-nitrobenzyl)-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(4-trifluoromethylbenzyl)-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(2,4-dichlorobenzyl)-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(2-phenylethyl)-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(2-phenylethenyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(benzoylmethyl)-N-(4-quinolinylmethyl)-4-piperidineamine;

(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(4-chlorobenzoylmethyl)-N-(4-quinolinyl-methyl)-4-piperidineamine;
(2R,4S)-N-[1-(3,5-Bistrifluoromethylbenzoyl)-2-benzyl-4-piperidinyl]quinoline-4-carboxamide;
(2R,4S)-N-[1-(3,5-Bistrifluoromethylbenzoyl)-2-benzylpiperidinyl]quinazoline-4-carboxamide;
(2R,4S)-N-[1-(3,5-Bistrifluoromethylbenzoyl)-2-(4-chlorobenzyl)-4-piperidinyl]quinoline-4-carboxamide;
(2R,4S)-N-[1-(3,5-Bistrifluoromethylbenzoyl)-2-(4-chlorobenzyl)piperidinyl]quinazoline-4-carboxamide;
(2R,4S)-N-[1-(3,5-Bistrifluoromethylbenzoyl)-2-(4-chlorobenzyl)piperidinyl]isoquinoline-1-carboxamide;
(2R,4S)-N-[1-(3,5-Bistrifluoromethylbenzoyl)-2-(4-nitrobenzyl)piperidinyl]quinazoline-4-carboxamide;
or a salt thereof in each case.

The compounds of the formula (I) for the novel use can be used, for example, in the form of pharmaceutical products which comprise a therapeutically effective amount of the active substance, with or without inorganic or organic, solid or liquid, pharmaceutically utilizable vehicles suitable for enteral, for example oral, or parenteral administration. Thus, tablets or gelatin capsules which have the active substance together with diluents, for example lactose, dextrose, sucrose, mannitol, sorbitol, cellulose and/or lubricants, for example diatomaceous earth, talc, stearic acid or salts thereof, such as magnesium or calcium stearate, and/or polyethylene glycol. Tablets may likewise have binders, for example magnesium aluminium silicate, starches such as maize, wheat, rice or arrowroot starch, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose and/or polyvinylpyrrolidone and, if required, disintegrants, for example starches, agar, alginic acid or a salt thereof, for example sodium alginate, and/or effervescent mixtures, or absorbents, dyes, flavourings and sweeteners. It is furthermore possible for the novel compounds of the formula (I) to be used in the form of products which can be administered parenterally or of infusion solutions. Solutions of this type are preferably isotonic aqueous solutions or suspensions, it being possible to prepare the latter, for example in the case of lyophilized products which comprise the active substance alone or together with an excipient, for example mannitol, before use. The pharmaceutical products can be sterilized and/or comprise ancillary substances, for example preservatives, stabilizers, wetting agents and/or emulsifiers, solubilizers, salts to control the osmotic pressure and/or buffers. The present

pharmaceutical products which, if required, may comprise further pharmacologically active substances, are produced in a manner known per se, for example by conventional mixing, granulating, coating, dissolving or lyophilizing processes, and comprise from about 0.1% to 100%, in particular from about 1% to about 50%, lyophilizates up to about 100%, of the active substance.

The dosage may depend on various factors such as mode of administration, species, age and/or individual condition. The doses to be administered each day are between about 0.25 and about 10 mg/kg, and for warm-blooded species with a bodyweight of about 70 kg preferably between about 20 mg and about 500 mg, on oral administration.

Example 1: Tablets, each comprising e.g. 50 mg of (2R,4S)-2-benzyl-1-(3,5-dimethylbenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine or a pharmaceutically acceptable salt, for example the dihydrochloride, thereof, can be prepared as follows:

| Composition (10 000 tablets) | |
|---|---|
| active ingredient | 500.0 g |
| lactose | 500.0 g |
| potato starch | 352.0 g |
| gelatin | 8.0 g |
| talc | 60.0 g |
| magnesium stearate | 10.0 g |
| silicon dioxide (highly dispersed) | 20.0 g |
| ethanol | q.s. |

The active ingredient is mixed with the lactose and 292 g of potato starch and the mixture is moistened with an ethanolic solution of the gelatin and granulated through a sieve. After drying, the remainder of the potato starch, the magnesium stearate, the talc and the silicon dioxide are mixed in and the mixture is compressed to form tablets, each weighing 145.0 mg and comprising 50.0 mg of active ingredient; the tablets may, if desired, be provided with breaking notches for finer adaptation of the dose.

Example 2: Film-coated tablets, each comprising 100 mg of (2R,4S)-2-benzyl-1-(3,5-dimethylbenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine or a pharamceutiacally acceptable salt, for example the dihydrochloride, thereof, can be prepared as follows:

| Composition (for 1000 film-coated tablets) | |
|---|---|
| active ingredient | 100.0 g |
| lactose | 100.0 g |
| corn starch | 70.0 g |
| talc | 8.5 g |
| calcium stearate | 1.5 g |
| hydroxypropylmethylcellulose | 2.36 g |
| shellac | 0.64 g |
| water | q.s. |
| methylene chloride | q.s. |

The active ingredient, the lactose and 40 g of the corn starch are mixed and moistened with a paste prepared from 15 g of corn starch and water (with heating) and granulated. The granules are dried, the remainder of the corn starch, the talcum and the calcium stearate are added and mixed with the granules. The mixture is compressed to form tablets (weight: 280 mg) which are then film-coated with a solution of the hydroxypropylmethylcellulose and the shellac in methylene chloride; final weight of the film-coated tablet: 283 mg.

Example 3: Hard gelatin capsules, comprising 100 mg of active ingredient, for example. (2R,4S)-2-benzyl-1-(3,5-dimethylbenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine or a pharmaceutically acceptable salt, for example the dihydrochloride, thereof, can be prepared, for example, as follows:

| Composition (for 1000 capsules) | |
|---|---|
| active ingredient | 100.0 g |
| lactose | 250.0 g |
| microcrystalline cellulose | 30.0 g |
| sodium lauryl sulfate | 2.0 g |

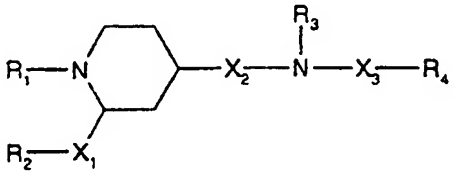
magnesium stearate 8.0 g

The sodium lauryl sulfate is added to the lyophilised active ingredient through a sieve of 0.2 mm mesh size. The two components are intimately mixed. Then first the lactose is added through a sieve of 0.6 mm mesh size and then the microcrystalline cellulose is added through a sieve of 0.9 mm mesh size. The mixture is then intimately mixed again for 10 minutes. Finally the magnesium stearate is added through a sieve of 0.8 mm mesh size. After mixing for a further 3 minutes, size 0 hard gelatin capsules are each filled with 390 mg of the resulting formulation.

WHAT IS CLAIMED IS:

1. The use of a substance P antagonist for producing pharmaceutical products for the treatment of social phobia.

2. The use of a compound of the formula (I)



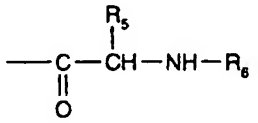
or of a pharmaceutically utilizable salt thereof, in which
$R_1$ is an unsubstituted or substituted aralkyl, aryloxyalkyl, heteroaralkyl, aroyl, heteroaroyl, cycloalkylcarbonyl, aralkanoyl, heteroarylalkanoyl, aralkoxycarbonyl or arylcarbamoyl radical or the acyl radical of an α-amino acid which is unsubstituted or N-substituted by lower alkanoyl or carbamoyl-lower-alkanoyl;
$R_2$ is cycloalkyl or an unsubstituted or substituted aryl or heteroaryl radical;
$R_3$ is hydrogen, alkyl, carbamoyl or an alkanoyl or alkenoyl radical which is unsubstituted or substituted by carboxyl or esterified or amidated carboxyl;
$R_4$ is an unsubstituted or substituted aryl or unhydrogenated or partially hydrogenated heteroaryl radical;
$X_1$ is methylene, ethylene, a direct linkage, a carbonyl group which may be ketalized, or an unetherified or etherified hydroxymethylene group;
$X_2$ is alkylene, carbonyl or a direct linkage; and
$X_3$ is carbonyl, oxo-lower-alkylene, oxo(aza)-lower-alkylene or an alkylene radical which is unsubstituted or substituted by phenyl, hydroxymethyl, carboxyl which may be esterified or amidated, or by hydroxyl in a position higher than α; according to claim for producing pharmaceutical products for the treatment of social phobia.

3. The use of a compound of the formula (I) or of a pharmaceutically utilizable salt thereof, in which $R_1$ is a phenyl-, diphenyl-, naphthyl- or fluorenyl-lower-alkyl radical which is unsubstituted or substituted in the phenyl moiety by lower alkyl, lower alkoxy, di-lower-alkylamino, halogen and/or trifluoromethyl, or a phenoxy-lower-alkyl radical which is unsubstituted or substituted in the phenyl moiety by halogen and/or triazolyl, or a heteroaryl-

lower-alkyl radical which has as heteroaryl radical an azaheteroaryl which is a 6-membered monocycle or a bicycle composed of a 6-membered and a 5- or 6-membered ring, or a benzoyl, naphthoyl, fluorenoyl or 3- to 8-membered cycloalkylcarbonyl radical which is unsubstituted or substituted by lower alkyl, lower alkoxy, hydroxyl, di-lower-alkylamino, halogen, cyano and/or trifluoromethyl, or a phenyl- or diphenyl-lower-alkanoyl radical which is unsubstituted or substituted in the phenyl moiety by lower alkyl, lower alkoxy, di-lower-alkylamino, halogen and/or trifluoromethyl, or a heteroaryl-lower-alkanoyl radical which has as heteroaryl radical an azaheteroaryl which is a 6-membered monocycle or a bi- or tricycle composed of a 6-membered and one or two 5- or 6-membered ring(s), or a phenyl-lower-alkoxycarbonyl or N-phenylcarbamoyl radical which is unsubstituted or substituted in the phenyl moiety by lower alkyl, lower alkoxy, di-lower-alkylamino or halogen and/or trifluoromethyl, or the acyl radical of an α-amino acid which is unsubstituted or N-substituted by lower alkanoyl or carbamoyl-lower-alkanoyl and occurs in nature as building block of peptides, $R_2$ is 5- to 7-membered cycloalkyl or a phenyl, naphthyl or 6-membered monocyclic azaheteroaryl radical which is unsubstituted or substituted by aromatically bonded lower alkyl, lower alkoxy, halogen and/or trifluoromethyl, $R_3$ is hydrogen, lower alkyl, carbamoyl, lower alkanoyl, carboxy-lower-alkanoyl or carboxy-lower-alkenoyl, lower alkoxycarbonyl-lower-alkyl, carbamoyl-lower-alkanoyl, N-mono- or N,N-di-lower-alkylcarbamoyl-lower-alkanoyl, N-cycloalkylcarbamoyl-lower-alkanoyl or N-phenylcarbamoyl-lower-alkanoyl, $R_4$ is a phenyl, naphthyl or pyridyl radical which is unsubstituted or substituted by lower alkyl, lower alkoxy, halogen and/or trifluoromethyl, or a heteroaryl radical which is unsubstituted or C-substituted by lower alkyl, lower alkoxy, halogen and/or trifluoromethyl and possibly N-substituted by lower alkanoyl and is composed of an unhydrogenated or partially hydrogenated 5- or 6-membered mono- or diaza- or oxaheteroaryl radical and a 6-membered aryl radical, $X_1$ is methylene, ethylene, a carbonyl group which may be ketalized by a lower alkanol or a lower alkanediol, or a hydroxy-methylene group which is unetherified or etherified with a lower alkanol, or a direct linkage, $X_2$ is carbonyl, lower alkylene or a direct linkage, and $X_3$ is carbonyl, oxo-lower-alkylene, oxo(aza)-lower-alkylene or a lower alkylene radical which is unsubstituted or substituted by phenyl or in position 1, 2 or, if present, 3 to the N atom by carboxyl, lower alkoxycarbonyl, carbamoyl, N-mono or N,N-di-lower-alkylcarbamoyl or hydroxymethyl; according to claim 2.

4. The use of a compound of the formula (I) or of a pharmaceutically utilizable salt thereof, in which

$R_1$ is phenyl- or diphenyl-$C_1$-$C_4$alkyl, which is unsubstituted or substituted in the phenyl moiety by lower alkyl, lower alkoxy, di-lower-alkylamino, halogen and/or trifluoromethyl, such as benzyl, 2,4-dichlorobenzyl, 3,5-ditrifluoromethylbenzyl, 2-phenylethyl or 2,2-diphenylethyl, or phenoxy-$C_1$-$C_4$alkyl, pyridyl- or quinolinyl-$C_1$-$C_4$alkyl, which is unsubstituted or substituted in the phenyl by halogen and/or triazolyl, such as 4-quinolinylmethyl, or benzoyl which is unsubstituted or substituted by lower alkyl, lower alkoxy, di-lower-alkylamino, halogen and/or trifluoromethyl, such as benzoyl, 3-lower-alkyl-, 3-lower-alkoxy-, 3-halo-, 3-dimethylamino-, 3,5-di-lower-alkyl-, 3,5-di-lower-alkoxy-, 3,5-dihalo- or 3,5-ditrifluoromethylbenzoyl, or secondarily naphthoyl which is unsubstituted or substituted by lower alkyl, lower alkoxy, di-lower-alkylamino, halogen and/or trifluoromethyl, such as 1- or 2-naphthoyl, or pyridylcarbonyl or quinolinylcarbonyl which is unsubstituted or substituted by lower alkyl, lower alkoxy, halogen and/or trifluoromethyl, or 5- to 7-membered cycloalkylcarbonyl which is unsubstituted or substituted by lower alkyl, lower alkoxy, di-lower-alkylamino, halogen and/or trifluoromethyl, such as cyclohexylcarbonyl, 3-methyl-, 3-methoxy-, 3-chloro-, 3-dimethylamino-, 3,5-dimethyl-, 3,5-dimethoxy-, 3,5-dichloro- or 3,5-ditrifluoromethylcyclohexylcarbonyl, or phenyl- or diphenyl-$C_1$-$C_4$alkanoyl which is unsubstituted or substituted in the phenyl by lower alkyl, lower alkoxy, di-lower-alkylamino, halogen and/or trifluoromethyl, such as 2,2-diphenylacetyl or 2,3-diphenylpropionyl, or N-phenylcarbamoyl which is unsubstituted or substituted in the phenyl moiety by lower alkyl, lower alkoxy, di-lower-alkylamino, halogen and/or trifluoromethyl, or a group of the formula (Ia)



(Ia)

in which $R_5$ is hydrogen, $C_1$-$C_4$alkyl which is unsubstituted or substituted by hydroxyl, mercapto, amino, unsubstituted or hydroxy-substituted phenyl, carboxyl, carbamoyl or ureido, and $R_6$ is $C_2$-$C_7$alkanoyl, $R_2$ is 5- to 7-membered cycloalkyl or a phenyl, naphthyl or pyridyl radical which is unsubstituted or substituted by $C_1$.$C_4$alkyl, $C_1$-$C_4$alkoxy, halogen and/or trifluoromethyl, $R_3$ is hydrogen, $C_1$.$C_7$alkyl, carbamoyl, $C_2$-$C_7$alkanoyl, carboxy-$C_1$.$C_4$alkanoyl or carboxy-$C_2$-$C_4$alkenoyl, $R_4$ is phenyl or naphthyl which is unsubstituted or substituted by $C_1$-$C_4$alkyl, $C_1$.$C_4$alkoxy, halogen and/or trifluoromethyl, or unsubstituted pyridyl, benzofuranyl, indolyl, 2,3-dihydroindolyl, benzimidazolyl, quinolyl or 1,2,3,4-tetra-

hydroquinolinyl, $X_1$ is methylene, hydroxymethylene, $C_1$-$C_4$alkoxymethylene, carbonyl or di-$C_1$-$C_4$-alkoxymethylene or a direct linkage, $X_2$ is $C_1$-$C_7$alkylene, carbonyl or a direct linkage, and $X_3$ is carbonyl, $C_1$-$C_4$alkylene, carboxy-$C_1$-$C_4$alkylene, $C_1$-$C_4$alkoxycarbonyl-$C_1$-$C_4$-alkylene, carbamoyl-$C_1$-$C_4$alkylene or hydroxymethyl-$C_1$-$C_4$alkylene; according to claim 2.

5. The use of a compound of the formula (I) or of a pharmaceutically utilizable salt thereof, in which

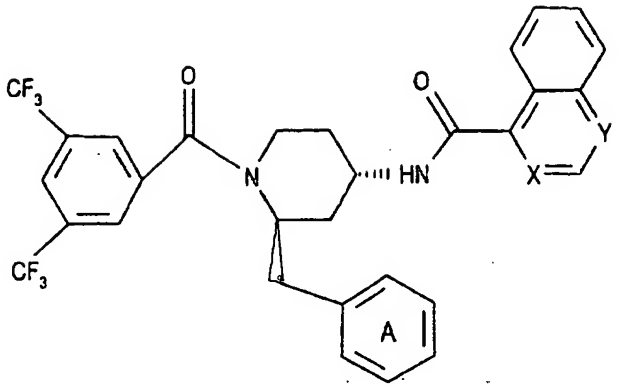
$R_1$ is benzoyl, naphthoyl or phenyl-$C_1$.$C_4$alkanoyl which is unsubstituted or substituted by $C_1$.$C_4$alkyl such as methyl, $C_1$.$C_4$alkoxy such as methoxy, halogen and/or trifluoromethyl, or unsubstituted pyridylcarbonyl or quinolinylcarbonyl, or a group of the formula (Ia) in which $R_5$ is hydrogen, $C_1$-$C_4$alkyl which is unsubstituted or substituted by hydroxyl, mercapto, amino, unsubstituted or hydroxyl-substituted phenyl, carboxyl, carbamoyl or ureido, for example methyl, isopropyl, isobutyl, secondary butyl, hydroxymethyl, mercaptomethyl, 2-methylmercaptoethyl, 3-ureidopropyl, 4-aminobutyl, carboxymethyl, carbamoylmethyl, 2-carboxyethyl, 2-carbamoylethyl, benzyl or 4-hydroxybenzyl, and $R_6$ is $C_2$-$C_7$alkanoyl such as acetyl, propionyl, butyryl or pivaloyl, $R_2$ is 5- to 7-membered cycloalkyl, in particular cyclohexyl, or secondarily cyclopentyl or cycloheptyl, or a phenyl, naphthyl or pyridyl radical which is unsubstituted or substituted by $C_1$-$C_4$alkyl such as methyl, $C_1$-$C_4$alkoxy such as methoxy, halogen and/or trifluoromethyl, $R_3$ is hydrogen, $C_1$-$C_7$alkyl such as methyl, ethyl, propyl, isopropyl or butyl, isobutyl, secondary butyl or tertiary butyl, carbamoyl, $C_2$-$C_7$alkanoyl such as acetyl, propionyl, butyryl or pivaloyl, carboxy-$C_1$-$C_4$alkanoyl such as succinoyl, glutaroyl or adipoyl, or carboxy-$C_3$-$C_5$alkenoyl such as maleyl, fumaroyl or tartroyl, $R_4$ is phenyl or naphthyl which is unsubstituted or substituted by $C_1$-$C_4$alkyl such as methyl, $C_1$-$C_4$alkoxy such as methoxy, halogen and/or trifluoromethyl, or unsubstituted pyridyl, benzofuranyl, indolyl, benzimidazolyl or quinolyl, $X_1$ is methylene, hydroxymethylene, $C_1$-$C_4$alkoxymethylene such as methoxymethylene, ethoxymethylene, propyloxymethylene or butyloxymethylene, carbonyl, di-$C_1$-$C_4$alkoxymethylene such as dimethoxymethylene, diethoxymethylene, dipropyloxymethylene or dibutyloxymethylene, or a direct linkage, $X_2$ is $C_1$-$C_7$alkylene such as methylene or secondarily ethylene or 1,3-propylene, carbonyl or a direct linkage, and $X_3$ is carbonyl, $C_1$-$C_4$alkylene such as methylene, ethylene or 1,3-propylene, carboxy-$C_1$-$C_4$alkylene such as 1,3-(2-carboxy)propylene, 1,4-(2-carboxy)-butylene, 1,4-(3-carboxy)butylene, $C_1$-$C_4$alkoxycarbonyl-$C_1$-$C_4$-alkylene such as 1,3-(2-$C_1$.$C_4$alkoxycarbonyl)propylene, 1,4-(2-$C_1$-$C_4$alkoxycarbonyl)butylene, 1,4-(3-$C_1$-$C_4$.alkoxycarbonyl)butylene, 1,5-(2-$C_1$-$C_4$alkoxycarbonyl)pentylene, 1,5-(3-$C_1$-$C_4$alkoxy-

carbonyl)pentylene or 1,5-(4-$C_1$-$C_4$alkoxycarbonyl)pentylene, where $C_1$-$C_4$alkoxycarbonyl is, in each case, for example methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl or butoxycarbonyl, or carbamoyl-$C_1$-$C_4$alkylene such as 1,3-(2-carbamoyl)propylene, 1,4-(2-carbamoyl)butylene, 1,4-(3-carbamoyl)butylene, 1,5-(2-carbamoyl)pentylene, 1,5-(3-carbamoyl)pentylene or 1,5-(4-carbamoyl)pentylene or hydroxymethyl-$C_1$-$C_4$alkylene, such as 1,3-(2-hydroxymethyl)propylene, 1,4-(2-hydroxymethyl)butylene, 1,4-(3-hydroxymethyl)butylene, 1,5-(2-hydroxymethyl)pentylene, 1,5-(3-hydroxymethyl)pentylene or 1,5-(4-hydroxymethyl)pentylene; according to claim 2.

6. The use of a compound of the formula (I) or of a pharmaceutically utilizable salt thereof, in which

$R_1$ is benzoyl which is unsubstituted or mono- or disubstituted by $C_1$-$C_4$alkyl such as methyl, $C_1$-$C_4$alkoxy such as methoxy, halogen of atomic number up to and including 35, such as chlorine, and/or trifluoromethyl, or unsubstituted naphthoyl or phenyl-$C_1$-$C_4$alkanoyl, $R_2$ is phenyl which is unsubstituted or substituted by $C_1$-$C_4$alkyl such as methyl, $C_1$-$C_4$alkoxy such as methoxy, halogen of atomic number up to and including 35, such as chlorine and/or trifluoromethyl, or unsubstituted pyridyl, $R_3$ is hydrogen, $C_1$-$C_4$alkyl such as methyl, ethyl, propyl or isopropyl, carbamoyl or $C_2$-$C_7$alkanoyl such as acetyl, propionyl, butyryl or pivaloyl, $R_4$ is phenyl which is unsubstituted or mono- or disubstituted by $C_1$-$C_4$alkyl such as methyl, $C_1$-$C_4$alkoxy such as methoxy, halogen of atomic number up to and including 35, such as chlorine and/or trifluoromethyl, or unsubstituted naphthyl, pyridyl, benzofuranyl, indolyl, benzimidazolyl or quinolyl, $X_1$ is methylene, hydroxymethylene, carbonyl or a direct linkage, $X_2$ is a direct linkage, and $X_3$ is $C_1$-$C_4$alkylene such as methylene or secondarily ethylene or 1,3-propylene; according to claim 2.

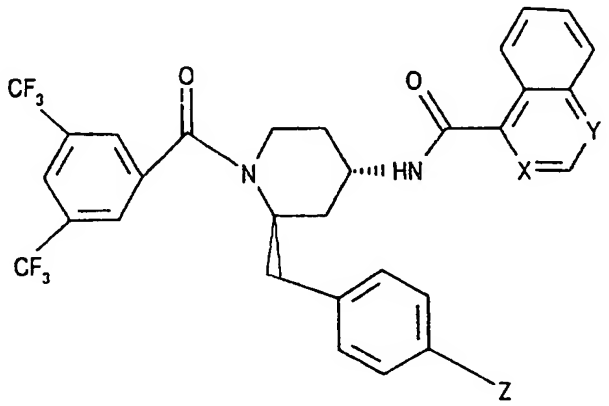
7. The use of a compound of the formula (Ib)




(Ib),

or of a pharmaceutically utilizable salt thereof, in which
X and Y are, independently of one another, N and/or CH, and ring A is unsubstituted or substituted one or more times by substituents selected from the group consisting of lower alkyl, lower alkoxy, halogen, nitro and trifluoromethyl; according to claim 2.

8. The use of a compound of the formula (Ic)




(Ic),

or of a pharmaceutically utilizable salt thereof, in which X is N or CH and Y is N; and Z is halogen such as chlorine; according to claim 2.

9. The use of a compound of the formula (Ic) or of a pharmaceutically utilizable salt thereof, in which X is N or CH and Y is N; and Z is halogen such as chlorine; according to claim 2.

10. The use of a compound of the formula (I) or of a pharmaceutically utilizable salt thereof, in which

$R_1$ is benzoyl which is unsubstituted or mono- or disubstituted by $C_1$-$C_4$alkyl such as methyl, $C_1$-$C_4$alkoxy such as methoxy, halogen of atomic number up to and including 35, such as chlorine, and/or trifluoromethyl, or unsubstituted naphthoyl, $R_2$ is phenyl which is unsubstituted or mono- or disubstituted by halogen of atomic number up to and including 35, such as chlorine, and/or trifluoromethyl, $R_3$ is hydrogen, $R_4$ is unsubstituted quinolyl, $X_1$ is methylene, $X_2$ is a direct linkage, and $X_3$ is $C_1$-$C_4$alkylene such as methylene or secondarily ethylene or 1,3-propylene; according to claim 2.

11. The use of a compound of the formula (I) or of a pharmaceutically utilizable salt thereof according to claim 2, selected from the group consisting of:
(2R*,4S*)-2-Benzyl-1-(2-naphthoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3-trifluoromethylbenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-bis-(trifluoromethyl)-benzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(1-naphthoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(2-quinolinoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(4-chloro-phenylacetyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(benzyloxycarbonyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(2-phenylethyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(2-naphthylacetyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(4-quinolylmethyl)-N-(4-quinolylmethyl)-4-piperidineamine or a salt thereof.
(2R*,4S*)-2-Benzyl-1-(2,4-dichlorobenzyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(2,2-diphenylethyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(phenylcarbamoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(diphenylacetyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(2-pyridylacetyl)-N-(4-quinolylmethyl)-4-piperidineamine;

(2R*,4S*)-2-Benzyl-1-(4-pyridylacetyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(2,3-diphenylpropionyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-((3S)-(2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-3-yl)-carbonyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3-methoxybenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3-N,N-dimethylaminobenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(cis,cis-3,5-dimethylcyclohexylcarbonyl)-N-(4-quinolyl-methyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-bis-(trifluoromethyl)benzyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2S*,4R*)-2-Benzyl-1-(2-(5-chloro-(1H-1,2,4-triazol-1-yl)phenoxy)ethyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-((S)-phenylalanyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-((R)-phenylalanyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-((S)-N-acetylphenylalanyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-((R)-N-acetylphenylalanyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-((S)-N-(4-carbamoylbutyryl)phenylalanyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-((R)-N-(4-carbamoylbutyryl)phenylalanyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-benzoyl-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3-chlorobenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(4-quinolylmethyl)-N-(3-carbamoyl-propionyl)-4-piperidineamine;
(2R,4S)- or (2R,4R)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2S,4R) and (2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-phenethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-quinolylmethyl)-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-quinolylmethyl)-4-piperidineamine;
(2R/4S)- or (2R/4R)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-benzyl-4-piperidineamine;
(2S/4R)- or (2S/4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-benzyl-4-piperidineamine;
(2R/4S)- or (2R/4R)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-pyridylmethyl)-4-piperidineamine;
(2R/4S)- or (2R/4R)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-pyridylmethyl)-4-piperidineamine;
(2S,4R)- and (2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-benzyl-N-carbamoyl-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-phenylpropyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-phenylpropyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-methoxybenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-methoxybenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2-methoxyphenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2-methoxyphenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2-methoxyphenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2-methoxyphenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-trifluoromethylbenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-trifluoromethylbenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2-trifluoromethylphenyl)ethyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2-trifluoromethylphenyl)ethyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2-trifluoromethylphenyl)propyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2-trifluoromethylphenyl)propyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-trifluoromethylbenzyl)-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-trifluoromethylbenzyl)-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(3-trifluoromethylphenyl)ethyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(3-trifluoromethylphenyl)ethyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(3-trifluoromethylphenyl)propyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(3-trifluoromethylphenyl)propyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-trifluoromethylbenzyl)-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-trifluoromethylbenzyl)-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(4-trifluoromethylphenyl)ethyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(4-trifluoromethylphenyl)ethyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(4-trifluoromethylphenyl)propyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(4-trifluoromethylphenyl)propyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,3-dimethoxybenzyl)-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,3-dimethoxybenzyl)-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,3-dimethoxyphenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,3-dimethoxyphenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,3-dimethoxyphenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,3-dimethoxyphenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,4-dimethoxybenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,4-dimethoxybenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,4-dimethoxyphenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,4-dimethoxyphenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,4-dimethoxyphenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,4-dimethoxyphenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,5-dimethoxybenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,5-dimethoxybenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,5-dimethoxyphenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,5-dimethoxyphenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,5-dimethoxyphenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,5-dimethoxyphenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,6-dimethoxybenzyl)-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,6-dimethoxybenzyl)-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,6-dimethoxyphenyl)ethyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,6-dimethoxyphenyl)ethyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,6-dimethoxyphenyl)propyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,6-dimethoxyphenyl)propyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,3-methylenedioxybenzyl)-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,3-methylenedioxybenzyl)-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,3-methylenedioxyphenyl)ethyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,3-methylenedioxyphenyl)ethyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,3-methylenedioxyphenyl)propyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,3-methylenedioxyphenyl)propyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,4-methylenedioxybenzyl)-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2,4-methylenedioxybenzyl)-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,4-methylenedioxyphenyl)ethyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2,4-methylenedioxyphenyl)ethyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,4-methylenedioxyphenyl)propyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2,4-methylenedioxyphenyl)propyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-indolylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-quinolinylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-quinolinylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-methoxy-1-naphthylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-methoxy-1-naphthylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-indolylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-quinolinylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-quinolinylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-quinolinylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-quinolinylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-methoxy-1-naphthylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-methoxy-1-naphthylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-indolylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-quinolinylmethyl)-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-quinolinylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-quinolinylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-methoxy-1-naphthylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(4-methoxy-1-naphthylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(2-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(2-indolylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(2-quinolinylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(2-quinolinylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(3-quinolinylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(3-quinolinylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(2-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(2-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(3-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(3-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(4-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(4-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(4-methoxy-1-naphthyl-methyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(4-methoxy-1-naphthyl-methyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-ditrifluoromethylbenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(2-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(2-indolylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(2-quinolinylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(2-quinolinylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3-quinolinylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3-quinolinylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(2-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(2-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3-chlorobenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(4-chlorobenzyl)-4-piperidineamine;

(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(4-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(4-methoxy-1-naphthylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(4-methoxy-1-naphthylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(2-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(2-indolylmethyl)-4--piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(3-indolylmethyl)-4--piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(2-quinolinylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(2-quinolinylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(3-quinolinylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(3-quinolinylmethyl)-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(2-chlorobenzyl)-4--piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(2-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[2-(2-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[3-(2-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(3-chlorobenzyl)-4--piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(3-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[2-(3-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[3-(3-chlorophenyl)propyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(4-chlorobenzyl)-4--piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(4-chlorobenzyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[2-(4-chlorophenyl)ethyl]-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-[3-(4-chlorophenyl)propyl]-4-piperidineamine;

(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(4-methoxy-1-naphthylmethyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(4-methoxy-1-naphthylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;
(2S,4S)-2-Benzyl-1-(3,5-dimethoxybenzoyl)-N-(3,4-ethylenedioxybenzyl)-4-piperidineamine;
(2R,4S) and (2R,4R)-2-Benzyl-1-(3,5-dimethylbenzoyl)-N-(2-phenethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-bis-(trifluoromethyl)benzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R,4S)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(2,4-dichlorobenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(phenylacetyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(2,6-dichlorobenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dibromobenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(9-fluorenoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3-toluoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3-bromobenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dihydroxybenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3-cyanobenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(2-chlorobenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(4-chlorobenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(9-fluorenyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(4-quinolylmethyl)-N-methyl-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(4-quinolylmethyl)-N-cyclohexyl-carbamoyl-4-piperidineamine;

(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(4-quinolylmethyl)-N-phenylcarbamoyl-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(2-phenylethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-bis-(trifluoromethyl)benzoyl)-N-(2-phenylethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(2-naphthoyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3,5-dimethylbenzoyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(4-quinolylcarbonyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3-indolylcarbonyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(2-indolylcarbonyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(5-methoxy-2-indolylcarbonyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(1-naphthoyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(phenylacetyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(2-methoxybenzyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-((N-acetyl)-3-indolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(2-benzo[b]furanylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-((3-methyl)-2-benzo[b]thiophenyl-methyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-((5-methoxy)-3-indolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3-indolylmethyl)-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-phenylcarbamoyl-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-diphenylmethyl-4-piperidineamine;
(2R*,4S*)-2-Benzyl-1-(3,5-dichlorobenzoyl)-N-(3,4-dihydro-2H-1-benzopyran-2-carbonyl)-4-piperidineamine;

(2R*,4S*)-2-Benzyl-1-(4-methoxybenzoyl)-N-(4-quinolylmethyl)-4-piperidineamine;
(2R*,4S*,1'R*)-N-Benzyl-1-(3,5-dimethylbenzoyl)-2-(1'-hydroxy-1'-phenylmethyl)--4-piperidineamine;
(2R*,4S*,1'R*)-2-(1'-hydroxy-1'-phenylmethyl)-1-(3,5-dimethylbenzoyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*,1'S*)-1-(3,5-Dimethylbenzoyl)-2-(1'-hydroxy-1'-phenylmethyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*,1'R*)-2-{1'-Hydroxy-1'-(4-chlorophenyl)methyl}-1-(3,5-dimethylbenzoyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*,1'S*)-1-(3,5-Dimethylbenzoyl)-2-{1'-hydroxy-1'-(4-chlorophenyl)-methyl}-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*,1'S*)-1-(3,5-Dimethylbenzoyl)-2-{1'-hydroxy-1'-(3,4-dichlorophenyl)-methyl}-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*,)-N-Benzyl-1-(3,5-dimethylbenzoyl)-2-benzoyl-4-piperidineamine;
(2R*,4S*)-2-(4-Chlorobenzyl)-1-(3,5-dimethylbenzoyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-2-(3,4-Dichlorobenzyl)-1-(3,5-dimethylbenzoyl)-N-(4-quinolinylmethyl)--4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-phenyl-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dichlorobenzoyl)-2-phenyl-N-(4-quinolinmethyl)-4-piperidineamine;
(2R*,4S*)-1-(1-Naphthoyl)-2-phenyl-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(1-naphthyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(2-naphthyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(4-methoxyphenylmethyl)-N-(4-quinolinyl-methyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(3-methoxyphenylmethyl)-N-(4-quinolinyl-methyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(4-nitrobenzyl)-N-(4-quinolinylmethyl)-4-piperidineamine;

(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(4-trifluoromethylphenylmethyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(2,4-dichlorophenylmethyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(2-phenylethyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(2-phenylethenyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-benzoyl-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(4-chlorobenzoyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(2-naphthyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(4-methoxybenzyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(3-methoxybenzyl)-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(4-nitrobenzyl)-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(4-trifluoromethylbenzyl)-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(2,4-dichlorobenzyl)-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(2-phenylethyl)-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(2-phenylethenyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(benzoylmethyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R*,4S*)-1-(3,5-Dimethylbenzoyl)-2-(4-chlorobenzoylmethyl)-N-(4-quinolinylmethyl)-4-piperidineamine;
(2R,4S)-N-[1-(3,5-Bistrifluoromethylbenzoyl)-2-benzyl-4-piperidinyl]quinoline-4-carboxamide;

(2R,4S)-N-[1-(3,5-Bistrifluoromethylbenzoyl)-2-benzyl-4-piperidinyl]quinazoline-4-carboxamide;
(2R,4S)-N-[1-(3,5-Bistrifluoromethylbenzoyl)-2-(4-chlorobenzyl)-4-piperidinyl]quinoline-4-carboxamide;
(2R,4S)-N-[1-(3,5-Bistrifluoromethylbenzoyl)-2-(4-chlorobenzyl)piperidinyl]quinazoline-4-carboxamide;
(2R,4S)-N-[1-(3,5-Bistrifluoromethylbenzoyl)-2-(4-chlorobenzyl)piperidinyl]isoquinoline-1-carboxamide; and
(2R,4S)-N-[1-(3,5-Bistrifluoromethylbenzoyl)-2-(4-nitrobenzyl)piperidinyl]quinazoline-4-carboxamide.

12. A pharmaceutical composition for the treatment of social phobia comprising a compound according to any one of claims 1-11 or a pharmaceutically acceptable salt thereof.

13. A method of treatmenf of social phobia in warm-blooded animals including man comprising administering to an individual in need of such treatment a therapeutically effective amount of a compound according to any one of claims 1-11 or a pharmaceutically acceptable salt thereof.

# INTERNATIONAL SEARCH REPORT

Inter: nal Application No
PCT/EP 97/02481

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K31/47 A61K31/445 A61K31/505

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| P,X | WO 96 24353 A (LILLY CO ELI ;JOHNSON KIRK W (US); PHEBUS LEE A (US)) 15 August 1996<br>see abstract<br>see page 3, line 12 - page 5, line 31<br>see page 21, line 17 - page 26, line 20<br>see page 63, line 1 - line 15<br>see page 66, line 8 - line 16; claims<br>--- | 1,12,13 |
| P,X | WO 96 29317 A (MERCK SHARP & DOHME ;OWENS ANDREW PATE (GB)) 26 September 1996<br>see abstract<br>see page 4, line 7 - line 8<br>see page 15, line 10 - line 24; claims<br>--- | 1,12,13 |
| | -/-- | |

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 22 September 1997 | 13.10.97 |

| Name and mailing address of the ISA | Authorized officer |
|---|---|
| European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. ( + 31-70) 340-2040, Tx. 31 651 epo nl,<br>Fax: ( + 31-70) 340-3016 | Hoff, P |

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# INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/EP 97/02481

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| P,X | WO 96 29328 A (MERCK SHARP & DOHME ;HAWORTH KAREN ELIZABETH (GB); OWEN SIMON NEIL) 26 September 1996<br>see abstract<br>see page 4, line 9 - line 10<br>see page 15, line 10 - line 24; claims | 1,12,13 |
| X | WO 93 14084 A (GLAXO GROUP LTD) 22 July 1993<br>see abstract<br>see page 1, line 6 - line 9<br>see page 4, line 20 - line 23<br>see page 6, line 20 - page 7, line 16<br>see page 34, line 5 - page 35, line 6; claims | 1,12,13 |
| X | EP 0 532 456 A (CIBA GEIGY AG) 17 March 1993<br>cited in the application<br>see abstract | 12 |
| Y | see page 4, line 55 - page 5, line 24<br>see page 15, line 34 - page 16, line 1; claims | 1-6,10, 11,13 |
| X | EP 0 707 006 A (CIBA GEIGY AG) 17 April 1996<br>see abstract | 12 |
| Y | see page 2, line 49 - page 3, line 58<br>see page 8, line 18 - line 42; claims; examples | 1-5,7-9, 11,13 |
| Y | "THE MERCK MANUAL" 1987 , MERCK SHARP & DOHME RESEARCH LABORATORIES XP002041393<br>see page 1504 - page 1505 | 1-11,13 |

1

# INTERNATIONAL SEARCH REPORT

Inte tional application No.
PCT/EP 97/02481

**Box I Observations where certain claims were found unsearchable (Continuation of item 1 f first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claim(s) 13
is(are) directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [X] Claims Nos.: 1-6,10,12-13
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

In view of the large number of compounds which are theoretically contained within the definition "substance P antagonist" and defined by the general formula of claim 2, the search was limited to the inventive part of the molecules and to the compounds mentioned in claim 11.

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. nal Application No
PCT/EP 97/02481

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---|---|---|
| WO 9624353 A | 15-08-96 | AU 4918796 A | 27-08-96 |
| WO 9629317 A | 26-09-96 | AU 5009796 A | 08-10-96 |
| WO 9629328 A | 26-09-96 | AU 5009896 A | 08-10-96 |
| WO 9314084 A | 22-07-93 | AU 3351393 A | 03-08-93 |
| EP 0532456 A | 17-03-93 | AT 120456 T | 15-04-95 |
| | | AU 660180 B | 15-06-95 |
| | | AU 2096592 A | 04-03-93 |
| | | CA 2075684 A | 13-02-93 |
| | | DE 59201771 D | 04-05-95 |
| | | ES 2070617 T | 01-06-95 |
| | | FI 964117 A | 14-10-96 |
| | | HU 67088 A | 30-01-95 |
| | | JP 7196649 A | 01-08-95 |
| | | NO 973117 A | 15-02-93 |
| | | NZ 243888 A | 26-03-96 |
| | | US 5541195 A | 30-07-96 |
| | | US 5646144 A | 08-07-97 |
| | | US 5310743 A | 10-05-94 |
| EP 0707006 A | 17-04-96 | AU 3317495 A | 26-04-96 |
| | | CA 2160444 A | 15-04-96 |
| | | CN 1133839 A | 23-10-96 |
| | | FI 954829 A | 15-04-96 |
| | | HU 74103 A | 28-11-96 |
| | | JP 8176145 A | 09-07-96 |
| | | NO 954067 A | 15-04-96 |
| | | ZA 9508647 A | 15-04-96 |